Supplementary file for the <u>manuscript thoraxjnl-2015-206938.R1</u>
"Characteristics of COPD in Never-smokers and Ever-smokers in the general population: results from the CanCOLD study."

<u>Definitions</u>

1. **Occupational exposure** was evaluated by asking participants whether they had worked ≥ 3 months and the number of years spent in each occupation suspected to be associated with risk of COPD. For analysis, occupational exposure was grouped in 3 categories:
   a. organic dust (eg farming ; forestry and fish-processing);
   b. inorganic (eg asbestos, hard rock mining);
   c. irritant gases/fumes/vapours (e.g firefighting, chemical or plastic manufacturing).

2. **A respiratory "exacerbation**" = Yes to question "ever had a period when breathing problems got so bad that they interfered with usual daily activities or resulted in missing work?"

<u>Spirometry Testing:</u>

Spirometry was performed by trained and certified technicians using the ndd Easyone spirometer (ndd Medical Technologies, Zurich, Switzerland). before and 15 minutes after two puffs of salbutamol (200ug) administered from a metered dose inhaler via a volumatic spacer. The quality of all tests was reviewed centrally in the CanCOLD study pulmonary function reference center in Vancouver, Canada.

Variables explained

Variable	Explanation
Education	How many years of schooling have you completed?
Childhood hospitalization	Were you hospitalized as a child for breathing problems prior to the age of 10?
HD/HT/DM	Has a doctor or other care provider ever told you that you had heart disease, hypertension or diabetes?
Asthma	Has a doctor or other health care provider ever told you that you have asthma, asthmatic bronchitis or allergic bronchitis?
Pack years	# of packs (20 cigarettes/pack) per day multiplied by number of smoking years
Pack years (categorical)	0=never,1=0-<10,2=10-<20,3=20+
Organic dust	Have you ever worked for 3 months or more at any of the following occupation? Flour, feed or grain milling; cotton or jute processing; farming; forestry; saw-milling.
Inorganic dust	Have you ever worked for 3 months or more at any of the following occupation? Hard rock mining; coal mining; sandblasting; working with asbestos; foundry or steel milling.
Gas/vapours	Have you ever worked for 3 months or more at any of the following occupation? Chemical or plastics manufacturing; welding; fire fighting; oil drilling; gas well.
Tuberculosis	Has a doctor or other care provider ever told you that you had tuberculosis?
Chronic cough	Do you cough on most days for as much as three months each year and has this cough for more than 2 years?
Chronic phlegm	Do you bring up the phlegm on most days for as much as three months each year and has this phlegm for more than 2 years?
Wheeze	Have you had this wheezing or whistling in your chest at any time in the last 12 months?
Dysnoea score	Are you unable to walk due to a condition other than shortness of breath? If yes, no dysnea score. If no, dysnea score is 1. And answer the following questions: are you troubled by shortness of breath when hurrying on the level or walking up a slight hill? If yes, dyspnea score=2. Do you have a walk slower than people of your age on level ground because of shortness of breath or do you ever have to stip for breath when walking at your own pace on level ground? If yes, dyspnea score=3. Do you ever have to stop for breath after walking about 100 yards (or after afew minutes) on level ground? If yes, score=4. Are you too short of breath to leave the house or short of breath on dressing or undressing? If yes, score=5.
Dysnea on exertion	If score>=2 then yes.
COPD	Has a doctor or other care provider ever told you that you had COPD?
Chronic bronchitis	Has a doctor or other care provider ever told you that you had chronic bronchitis?
Emphysema	Has a doctor or other care provider ever told you that you had emphysema?
Stroke	Has a doctor or other care provider ever told you that you had stroke?
Worked in any dusty job >1 yr	Have you ever worked for a year or more in a dusty job?

Biomass fuel exposure

Biomass fuel questionnaire used in this study was the same standardized and validated questionnaire that was used in the BOLD initiative and administered face-to-face by trained and accredited researcher coordinators according to the BOLD protocol for eliciting questionnaire responses, the results of which had been widely published. In this study, we had defined the presence of biomass fuel exposure for cooking and for heating in a conservative way as follows:

Biomass cooking:
1. Has an indoor open fire with coal or coke been used in your home as a primary means of cooking for more than 6 months in your life?
2. For how many years has coal or coke been used for cooking in your home?
3. Has an indoor open fire with wood, crop residues or dung been used in your home as a primary means of cooking for more than 6 months in your life?
4. For how many years have wood, crop residues or dung been used for cooking in your home?

Code:
If Question1=yes **and** Question2>=9 **then** biomass cooking=yes; **or**
If Question3=yes **and** Question4>=9 **then** biomass cooking=yes.
Otherwise biomass cooking=no.

Biomass heating:
1. Have you used an open fire with coal or coke as a primary means of heating your home for more than 6 months in your life?
2. For how many years have you used an open fire with coal or coke as a primary means of heating your home?
3. Have you used an open fire with wood, crop residues or dung as a primary means of heating your home for more than 6 months in your life?
4. For how many years have you used an open fire with wood, crop residues or dung as a primary means of heating your home?

Code:
If Question1=yes **and** Question2>=9 **then** biomass heating=yes; **or**
If Question3=yes **and** Question4>=9 **then** biomass heating=yes.
Otherwise biomass heating=no.

Statistic analysis- Holm-Bonferroni correction

Multiple hypotheses testing was corrected using the Holm-Bonferroni correction (Ref: Van Bell G, Fisher L, Heagerty P, Lumley T. Multiple Comparisons In Biostatistics: A Methodology for the Health Sciences. 2 ed. Seattle, Washington: Wiley-Interscience, 2004). The Holm-Bonferroni adjusted p-values were determined by ordering p-values from smallest to largest, with the smallest p-value multiplied by k, where k is the number of hypotheses to be tested. If the resulting modified p-value was less than α (Type I error rate) the hypothesis was rejected. The next smallest p-value was then multiplied by k-1 and the new modified p-value was compared to α. This process was repeated until the modified p-value could not be rejected.

Table S1 (complements Table 1 in manuscript): Demographics of never smokers and ever smokers by sex.

	Men			Women			
	Never Smokers n=891	**Ever Smokers n=1205**	**Adjusted P*£**	**Never Smokers n=1404**	**Ever Smokers n=1393**	**Adjusted P*£**	**Adjusted P**£**
Sex(men)	-	-	-	-	-	-	-
Ethnicity(Caucasian)	803(90.1%)	1118(92.8%)	0.1485	1216(86.6%)	1338(96.1%)	0.0015	0.0936
Age, yr, mean±sd	56.1(11.0)	58.8(11.4)	0.0015	57.1(11.3)	57.7(10.7)	0.3997	0.2485
Age			0.0014			0.8484	0.4218
40-49	296(33.2%)	306(25.4%)	-	406(28.9%)	366(26.3%)	-	-
50-59	284(31.9%)	352(29.2%)	-	466(33.2%)	459(33.0%)	-	-
60-69	190(21.3%)	316(26.2%)	-	311(22.2%)	358(25.7%)	-	-
70+	121(13.6%)	231(19.2%)	-	221(15.7%)	210(15.1%)	-	-
BMI, kg/m^2, mean±sd	27.7(4.7)	28.3(5.0)	0.0351	27.4(6.2)	28.3(6.7)	0.0132	0.0015
Education, yr, mean±sd	16.8(3.4)	15.0(3.7)	0.0013	15.6(3.5)	14.6(3.3)	0.0014	0.0014
Pack years>20	-	644(53.4%)		-	587(42.1%)		
Exposures							
Organic dust	118(13.2%)	166(13.8%)	1.0000	84(6.0%)	77(5.5%)	0.6052	0.0013
Inorganic dust	41(4.6%)	102(8.5%)	0.005	5(0.4%)	10(0.7%)	0.9515	0.0012
Gases/Vapours	72(8.1%)	124(10.3%)	0.3436	17(1.2%)	31(2.2%)	0.388	0.0011
Biomass fuel[#]							
≥10 years cooking	66(10.9%)	119(15.2%)	0.1337	129(12.7%)	107(11.5%)	0.8216	0.2196
≥10 years heating	84(13.9%)	149(19.0%)	0.0848	159(11.4%)	166(11.9%)	0.806	0.2232
Passive smoking at home	39(4.4%)	165(13.7%)	0.0012	67(4.8%)	196(14.1%)	0.0013	1.0000
Childhood hospitalization for respiratory illness	56(6.3%)	80(6.6%)	0.7602	55(3.9%)	93(6.7%)	0.0121	0.0846
Co-morbidities, ever							
HD/HT/DM[$]	287(32.2%)	534(44.3%)	0.0011	441(31.4%)	465(33.4%)	0.7962	0.6879
Asthma	113(12.7%)	129(10.7%)	0.4845	256(18.2%)	295(21.2%)	0.4527	0.004
Tuberculosis	6(0.7%)	22(1.8%)	0.1386	25(1.8%)	13(0.9%)	0.4232	0.1757

Data are mean(SD) or count(%). [*]P values of difference tests between never smokers and ever smokers; Kruskal-Wallis test (without assumption of normal distribution of data) and chi-squared test are used for continuous variables and categorical variables, respectively. [**]P values of difference tests between men and women in never smokers. [#]Calculated based on 6 sites with available biomass data. [$]Heart disease, systemic hypertension or diabetes. [£]p values adjusted by Holm-Bonferroni correction.

Table S2: Characteristics, respiratory symptoms, self-reported physician diagnoses and occupational & domestic dust, gases and smoke exposures of <u>never-smokers</u> (N=2295) stratified into 3 subgroups: without and with chronic airflow obstruction (defined by FEV1/FVC<LLN) graded further into mild and moderate-severe disease by FEV1 % predicted ≥80% or <80%

	NonCOPD (FEV1/FVC≥LLN)	COPD mild	COPD moderate
Subjects, No.(%)	2134	91(57%)	70(43%)$^\phi$
Age, yr, mean±sd	56.4±11.0	59.6±13.6	60.6±10.8**
Male gender	836(39.2)	27(29.7)	28(40.0)
Education, yr, mean±sd	16.1±3.5	15.6±4.0	15.2±3.4
BMI, kg/m^2, mean±sd	27.5±5.7	26.9±4.3	27.9±5.7
Respiratory Symptoms			
Chronic cough	181(8.5)	10(11.0)	20(28.6)**
Chronic phlegm	128(6.0)	11(12.1)	14(20.0)**
Wheezing	439(20.6)	30(33.0)	40(57.1)**
Dyspnea on exertion	402(18.8)	22(24.2)	34(48.6)**
Any of the above symptoms	816(38.2)	50(55.0)*	55(78.6)**
Ever had to leave a job due to breathing problems	63(3.0)	0(0)	6(8.6)
Physician diagnosis, ever			
Asthma	312(14.6)	25(27.5)*	32(45.7)**
COPD	13(0.6)	2(2.2)	7(10.1)**
Chronic bronchitis	55(2.6)	1(1.1)	11(15.9)**
Emphysema	9(0.4)	1(1.1)	2(2.9)
Any of the above diagnosis	347(16.3)	27(29.7)*	38(54.3)**
Tuberculosis	27(1.3)	2(2.2)	2(2.9)
HD/HT/DM$^\$$	673(31.5)	27(29.7)	28(40.0)
Stroke	45(2.1)	5(5.5)	0(0)
Childhood hospitalization for respiratory illness	90(4.2)	7(7.7)	14(20.3)**
Exposures			
Passive smoking at home	94(4.4)	8(8.8)	4(5.8)
Biomass cooking≥10 yrs$^\#$	178(11.7)	11(16.9)	6(13.0)
Biomass heating≥10 yrs$^\#$	221(14.6)	13(20.0)	11(23.9)
Organic dust	182(8.5)	14(15.4)	6(8.6)
Inorganic dust	41(1.9)	5(5.5)	0(0)
Gases/Vapours	79(3.7)	4(4.4)	6(8.6)
Worked in any dusty job >1 yr	504(23.6)	24(26.4)	19(27.5)

Data are mean±sd or count(%). $^\$$Heart disease, systemic hypertension or diabetes. $^\#$Calculated based on 6 sites with available biomass data. Significance measured on 5% level after Holm-Bonferroni correction; *COPD mild vs. NonCOPD; **COPD moderate-severe vs. NonCOPD. $^\phi$ significantly smaller proportion compared with ever smokers in Table S2.

Table S3: Characteristics, respiratory symptoms, self-reported physician diagnoses and occupational & domestic dust, gases and smoke exposures of <u>ever-smokers</u> (N=2598) stratified into 3 subgroups: without and with chronic airglow obstruction (defined by FVE1/FVC<LLN) graded further into mild and moderate-severe disease by FEV1 % predicted ≥80% or <80%

	NonCOPD (FEV1/FVC≥LLN)	COPD mild	COPD moderate
Subjects, No.(%)	2202	151(38%)	245(62%)$^{\phi}$
Age, yr, mean±sd	57.4±10.8	60.0±10.8*	64.4±11.3**
Male gender	1019(46.3)	73(48.3)	113(46.1)
Education, yr, mean±sd	15.0±3.4	14.7±3.7	13.5±3.5**
BMI, kg/m^2, mean±sd	28.3±6.0	27.1±4.9	28.4±6.2
Respiratory Symptoms			
Chronic cough	296(13.4)	30(19.8)	88(35.9)**
Chronic phlegm	219(10.0)	24(15.9)	79(32.2)**
Wheezing	680(30.9)	75(49.7)*	154(62.9)**
Dyspnea on exertion	545(24.8)	45(29.8)	122(49.8)**
Any of the above symptoms	1113(50.5)	106(70.2)*	203(82.9)**
Ever had to leave a job due to breathing problems	79(3.6)	3(2.0)	16(6.5)
Physician diagnosis, ever			
Asthma	303(13.8)	39(25.8)*	82(33.5)**
COPD	38(1.7)	10(6.6)*	52(21.2)**
Chronic bronchitis	114(5.2)	19(12.6)*	50(20.4)**
Emphysema	34(1.5)	6(4.0)	40(16.3)**
Any of the above diagnosis	394(17.9)	55(36.4)*	134(54.7)**
Tuberculosis	27(1.2)	3(2.0)	5(2.0)
HD/HT/DM$^{\$}$	815(37.0)	61(40.4)	123(50.2)**
Stroke	59(2.7)	2(1.3)	10(4.1)
Childhood hospitalization for respiratory illness	134(6.1)	15(10.0)	24(9.8)
Exposures			
Passive smoking at home	288(13.1)	31(20.5)	42(17.1)
Biomass cooking≥10 yrs$^{\#}$	181(12.7)	13(12.0)	32(18.4)
Biomass heating≥10 yrs$^{\#}$	256(17.9)	17(15.7)	40(23.0)
Organic dust	196(8.9)	13(8.6)	34(13.9)
Inorganic dust	91(4.1)	7(4.6)	14(5.7)
Gases/Vapours	126(5.7)	10(6.6)	19(7.8)
Worked in any dusty job >1 yr	679(30.8)	56(37.1)	105(42.9)**

Data are mean±sd or count(%). $^{\$}$Heart disease, systemic hypertension or diabetes. $^{\#}$Calculated based on 6 sites with available biomass data. Significance measured on 5% level after Holm-Bonferroni correction; *COPD mild vs. NonCOPD; **COPD moderate-severe vs. NonCOPD.$^{\phi}$significantly greater than that for never-smokers in table 2.

Table S4 (source for Fig 2,3,4 in manuscript): Comparison of Clinical, physiological and structural phenotypes of COPD (defined by LLN) in never-smokers with ever-smokers

	Never-smoker				Ever-smoker			
	NonCOPD	%	COPD	%	NonCOPD	%	COPD	%
N=835	**308**	-	**86**	-	**273**	-	**168**	-
Men	163	52.9	32	37.2*	152	55.7	77	45.8
Emphysema	32	10.4	11	12.8	71	26.0	92	54.8**;#
Emphysema score, mean(95% CI)	0.22 (0.14,0.30)	-	0.33 (0.08,0.57)	-	0.67 (0.50,0.83)	-	2.40**;# (1.91,2.89)	-
Bronchiolitis	23	7.5	10	11.6	44	16.1	26	15.5
Bronchiolitis score, mean(95% CI)	0.16 (0.09,0.22)	-	0.28 (0.11,0.45)	-	0.34 (0.25,0.44)	-	0.35 (0.22,0.47)	-
Bronchiectasis	65	21.1	23	26.7	58	21.3	40	23.8
N=4890	**2131**	-	**161**	-	**2202**	-	**396**	-
Dyspnea score, mean(95% CI)	1.28 (1.25,1.31)	-	1.57* (1.43,1.72)	-	1.39 (1.36,1.43)	-	1.88**;# (1.76,2.00)	-
Dyspnea on exertion	402	18.9	56	34.8*	545	24.8	167	42.2**
Wheeze	438	20.6	69	42.9*	680	30.9	229	57.8**;#
Chronic cough	181	8.5	30	18.6*	296	13.4	118	29.8**;#
Chronic Phlegm	128	6.0	25	15.5*	219	10.0	103	26.0**;#
Exacerbation	387	18.2	55	34.2*	450	20.4	112	28.3**
Asthma	312	14.6	57	35.4*	303	13.8	121	30.6**
N=977	**346**	-	**110**	-	**312**	-	**209**	-
BDR$_i$(%) mean(95% CI)	4.86 (4.47,5.25)		9.43* (7.68,11.18)		5.14 (4.46,5.63)		9.29** (8.09,10.43)	
VC(L) mean(95% CI)	3.78 (3.67,3.89)		3.62 (3.41,3.83)		3.64 (3.53,3.75)		3.56 (3.42,3.70)	
TLC(L) mean(95% CI)	5.95 (5.81,6.10)		6.10 (5.84,6.35)		5.95 (5.81,6.09)		6.39**;# (6.20,6.57)	
RV(L) mean(95% CI)	2.19 (2.13,2.25)		2.47* (2.33,2.61)		2.30 (2.24,2.37)		2.83**;# (2.72,2.94)	
FRC(L) mean(95% CI)	3.15 (3.06,3.23)		3.35 (3.19,3.51)		3.17 (3.09,3.26)		3.69**;# (3.57,3.82)	
ERV(L) mean(95% CI)	0.95 (0.89,1.01)		0.87 (0.77,0.96)		0.87 (0.81,0.92)		0.85 (0.78,0.91)	
IC(L) mean(95% CI)	2.81 (2.73,2.89)		2.73 (2.56,2.91)		2.77 (2.69,2.86)		2.70 (2.59,2.81)	
RAW(cmH$_2$O/L/sec) mean(95% CI)	2.20 (2.07,2.33)		3.28* (2.91,3.65)		2.41 (2.24,2.58)		3.22** (3.01,3.44)	
MIP(cmH$_2$O) mean(95% CI)	77.6 (74.6,80.7)		83.0 (76.1,89.9)		76.8 (73.6,80.0)		76.6 (72.6,80.5)	
MEP(cmH$_2$O) mean(95% CI)	110.0 (105.5,114.5)		116.6 (105.7,127.5)		108.9 (104.1,113.7)		110.5 (105.0,115.9)	
DLCO/VA(ml/min/mmHg/L) mean(95% CI)	4.15 (4.07,4.24)		4.12 (3.97,4.26)		3.92 (3.83,4.00)		3.64**;# (3.53,3.75)	
FRC/TLC(%) Mean(95% CI)	0.53 (0.52,0.54)		0.55* (0.54,0.57)		0.54 (0.53,0.54)		0.58**;# (0.57,0.59)	
DLCO(ml/min/mmHg) mean(95% CI)	21.60 (20.9,22.3)	-	21.60 (20.1,23.1)	-	20.40 (19.6,21.1)	-	18.74**;# (17.9,19.6)	-
RV/TLC(%) mean(95% CI)	0.37 (0.37,0.38)	-	0.41* (0.39,0.43)	-	0.39 (0.38,0.40)	-	0.45** (0.43,0.46)	-

Data are mean(95% CI) or count and %. *Significant difference between never-smoker NonCOPD and never-smoker COPD. **Significant difference between ever-smoker NonCOPD and ever-smoker COPD. #Significant difference between COPD never-smoker and COPD ever-smoker. P values adjusted after Holm-Bonferroni correction.
Exacerbation= Yes to question "ever had a period when breathing problems got so bad that they interfered with usual daily activities or resulted in missing work.

Table X2 (**detailed version of Table 2 in manuscript**) : aOR for independent predictors associated with risk of different severity of COPD defined by LLN in male and female never smokers

Variables	COPD mild			COPD moderate-severe		
	All N=2225	**Men** N=863	**Women** N=1362	**All** N=2204	**Men** N=864	**Women** N=1340
Sex	0.64(0.38,1.05)	-	-	1.21(0.70,2.09)	-	-
Age						
40-49	Ref	Ref	Ref	Ref	Ref	Ref
50-59	0.85(0.48,1.54)	0.87(0.28,2.70)	0.91(0.45,1.82)	2.52(1.17,5.44)*	4.13(1.12,15.2)*	1.78(0.67,4.71)
60-69	1.13(0.60,2.12)	0.48(0.11,2.04)	1.52(0.74,3.11)	3.15(1.41,7.02)*	5.38(1.35,21.3)*	2.27(0.82,6.28)
70+	2.19(1.15,4.16)*	2.50(0.77,8.16)	2.28(1.02,5.06)*	4.46(1.84,10.8)**	6.09(1.14,35.4)*	3.54(1.23,10.1)*
BMI	0.97(0.93,1.02)	0.98(0.89,1.08)	0.98(0.93,1.03)	0.98(0.93,1.03)	1.01(0.92,1.10)	0.97(0.92,1.03)
Education	0.98(0.92,1.04)	0.88(0.78,0.99)*	1.02(0.95,1.11)	0.95(0.88,1.02)	0.96(0.83,1.10)	0.94(0.86,1.03)
Exposures						
Organic dust	1.69(0.89,3.20)	2.08(0.81,5.33)	1.27(0.49,3.36)	0.85(0.35,2.09)	0.91(0.23,3.67)	0.92(0.27,3.16)
Inorganic dust	2.94(0.99,8.71)	3.24(0.99,10.57)	NC	NC	NC	NC
Gases/Vapours	0.92(0.30,2.83)	1.14(0.32,3.99)	NC	2.25(0.83,6.08)	2.40(0.69,8.41)	1.72(0.20,14.9)
Biomass fuel						
≥10 yrs cooking[#]	1.06(0.46,2.46)	0.70(0.16,2.98)	1.13(0.39,3.29)	0.67(0.23,1.94)	1.74(0.32,9.34)	0.55(0.18,1.65)
≥10 yrs heating[#]	0.88(0.39,1.96)	2.09(0.59,7.44)	0.62(0.21,1.82)	2.26(0.93,5.52)	0.44(0.08,2.42)	3.58(1.42,9.01)**
Passive smoking	2.18(0.99,4.75)	1.33(0.26,6.72)	2.60(1.05,6.43)*	1.25(0.42,3.73)	0.69(0.08,6.21)	1.65(0.46,5.88)
Childhood Hospitalization for respiratory illness	1.57(0.68,3.62)	2.95(0.84,10.4)	1.18(0.35,4.00)	4.80(2.43,9.46)****	10.1(3.71,27.5)****	2.24(0.73,6.84)
Co-morbidities, ever						
HD/HT/DM[$]	0.72(0.43,1.21)	1.55(0.61,3.95)	0.51(0.26,0.98)*	1.11(0.63,1.94)	1.48(0.57,3.90)	1.07(0.53,2.16)
Asthma	2.23(1.36,3.66)**	3.39(1.25,9.21)*	2.14(1.20,3.82)*	4.94(2.94,8.30)****	7.34(3.01,17.9)****	3.89(2.02,7.50)****
Tuberculosis	1.20(0.27,5.36)	NC	1.67(0.37,7.63)	1.64(0.35,7.69)	NC	2.02(0.41,9.79)

Data are adjusted odds ratios and 95% CI. Adjustment made for all other covariates in the model. [#]Calculated based on 6 sites with available biomass data. [$]Heart disease, hypertension or diabetes. Significant on different levels: *0.05; **0.01; ***0.001; ****≤0.0001. NC=counts too small for accurate estimate.

Table X3 (detailed version of Table 3 in manuscript): aOR for independent predictors associated with risk of different severity of COPD defined by LLN in male and female ever-smokers

Variables	COPD mild			COPD moderate-severe		
	All N=2353	**Men** N=1092	**Women** N=1261	**All** N=2447	**Men** N=1132	**Women** N=1315
Sex	1.17(0.84,1.67)	-	-	1.03(0.76,1.42)	-	-
Age						
40-49	Ref	Ref	Ref	Ref	Ref	Ref
50-59	1.40(0.84,2.31)	1.05(0.48,2.30)	1.65(0.85,3.21)	2.35(1.39,3.99)**	1.59(0.76,3.33)	3.42(1.57,7.43)**
60-69	2.21(1.31,3.75)*	3.02(1.40,6.52)**	1.66(0.80,3.45)	4.16(2.44,7.11)****	2.68(1.23,6.38)**	6.41(2.93,14.0)****
70+	3.01(1.66,5.46)****	4.19(1.75,10.0)***	2.23(0.96,5.21)	11.58(6.58,20.4)****	11.27(5.01,25.4)****	12.64(5.48,29.2)****
BMI	0.95(0.92,0.98)**	0.94(0.89,0.99)	0.95(0.91,0.99)*	0.99(0.96,1.01)	0.97(0.93,1.02)	0.99(0.96,1.02)
Current smoking (vs. former)	1.73(1.15,2.62)*	2.52(1.34,4.71)**	1.33(0.76,2.32)	2.89(2.04,4.10)****	3.61(2.04,6.38)****	2.53(1.61,3.98)****
Pack years						
0-10	Ref	Ref	Ref	Ref	Ref	Ref
10-20	2.03(1.18,3.49)*	2.07(0.86,4.96)	2.12(1.06,4.23)*	1.32(0.75,2.32)	0.86(0.34,2.14)	1.69(0.81,3.52)
20+	2.52(1.53,4.14)*	2.58(1.18,5.61)*	2.52(1.31,4.83)*	3.57(2.26,5.62)****	2.82(1.43,5.58)****	4.16(2.24,7.73)****
Education	1.00(0.96,1.05)	1.02(0.95,1.10)	0.98(0.91,1.05)	0.94(0.90,0.98)**	0.94(0.86,0.99)*	0.93(0.88,0.99)*
Exposures						
Organic dust	0.84(0.45,1.57)	0.90(0.43,1.89)	0.60(0.18,2.04)	1.36(0.86,2.13)	1.16(0.64,2.10)	1.73(0.83,3.60)
Inorganic dust	0.80(0.33,1.93)	0.75(0.28,2.01)	1.22(0.11,13.2)	0.65(0.32,1.29)	0.55(0.25,1.21)	1.45(0.23,9.12)
Gases/Vapours	0.98(0.47,2.05)	0.81(0.33,2.03)	1.29(0.34,4.88)	1.07(0.59,1.95)	1.34(0.67,2.67)	0.53(0.13,2.08)
Biomass fuel						
≥10 yrs cooking[#]	0.99(0.46,2.15)	0.42(0.13,1.35)	2.02(0.72,5.63)	0.81(0.44,1.48)	0.74(0.31,1.81)	0.83(0.35,1.96)
≥10 yrs heating[#]	0.65(0.33,1.28)	1.02(0.41,2.55)	0.44(0.16,1.17)	0.81(0.47,1.38)	0.72(0.32,1.63)	0.91(0.44,1.86)
Passive smoking at home	1.36(0.86,2.78)	1.50(0.77,2.93)	1.25(0.66,2.38)	1.12(0.59,1.34)	0.80(0.42,1.52)	0.95(0.55,1.36)
Childhood Hospitalization for respiratory illness	1.54(0.86,2.78)	1.34(0.52,3.44)	1.90(0.88,4.10)	1.65(0.98,2.77)	1.70(0.78,3.69)	1.51(0.73,3.12)
Co-morbidities, ever						
HD/HT/DM[$]	0.97(0.66,1.42)	0.85(0.49,1.48)	1.10(0.64,1.88)	0.98(0.71,1.34)	1.11(0.69,1.80)	0.87(0.57,1.35)
Asthma	2.51(1.67,3.76)****	2.74(1.41,5.33)**	2.25(1.33,3.82)**	3.82(2.72,5.35)****	4.58(2.64,7.95)****	3.22(2.08,4.96)****
Tuberculosis	1.70(0.50,5.85)	3.36(0.89,12.7)	NC	1.84(0.66,5.16)	1.54(0.39,6.09)	2.57(0.49,13.3)
Lung cancer	1.45(0.33,6.62)	0.94(0.11,8.12)	2.43(0.28,21.22)	2.85(1.06,7.66)	2.20(0.57,8.48)	3.79(0.90,16.00)

Data are adjusted odds ratios and 95% CI. Adjustment made for all other covariates in the model. [#]Calculated based on 6 sites with available biomass data. [$]Heart disease, hypertension or diabetes. Significant on different levels: *0.05; **0.01; ***0.001; ****≤0.0001.*HD/HT/DM is heart disease, systemic hypertension, or diabetes. NC=counts too small for accurate estimate.

Table S3.1: Comparison of sex, age and <u>respiratory medication use</u> of COPD (define by LLN) in never-smokers with ever-smokers

	Never-smoker				Ever-smoker			
	NonCOPD	**%**	**COPD**	**%**	**NonCOPD**	**%**	**COPD**	**%**
<u>**N=4890**</u>	**2131**	**-**	**161**	**-**	**2202**	**-**	**396**	**-**
Men	836	39.2	55	34.2	1019	46.3	186	47.0#
Age	56.4		60.0*		57.4		62.7*#	
(95% CI)	(56.0,56.9)	-	(58.1,61.9)	-	(56.9,57.8)	-	(61.6,63.8)	-
<u>**Use of respiratory medications**</u>	670	31.4	76	47.5*	665	32.0	190	48.0*
Prescribed medication	353	16.5	63	39.1*	378	17.2	156	39.4*
Bronchodilator	219	10.3	53	32.9*	235	10.7	138	34.9*
Inhaled steroid	279	13.1	53	32.9*	305	13.9	123	31.1*
Oral steroid	4	0.2	6	3.7*	9	0.4	1	0.3#
Anti-inflammatory (other)	10	0.5	6	3.7*	17	0.8	4	1.0
OTC§ medication	294	13.8	12	7.5*	259	11.8	31	7.8*

Data are count and % or mean(95%CI). *Significant difference between never-smoker NonCOPD and never-smoker COPD . **Significant difference between ever-smoker NonCOPD and ever-smoker COPD. #Significant difference between COPD never-smoker and COPD ever-smoker. P values adjusted after Holm-Bonferroni correction.

Comments: Respiratory Medication use was more frequent in COPD than in non-COPD individuals in both never-smokers and ever-smokers.

Figure S1: Weighted prevalence of COPD by sex and by severity of COPD and by two definitions [by FR(GOLD definition: FEV1/FVC<0.7) and by LLN (FEV1/FVC<5th percentile).] Key: M= men; F=women. Pale grey section = mild COPD(FEV1%pred ≥80%) ; Dark grey Column=moderate-severe(FEV1%pred<80%).
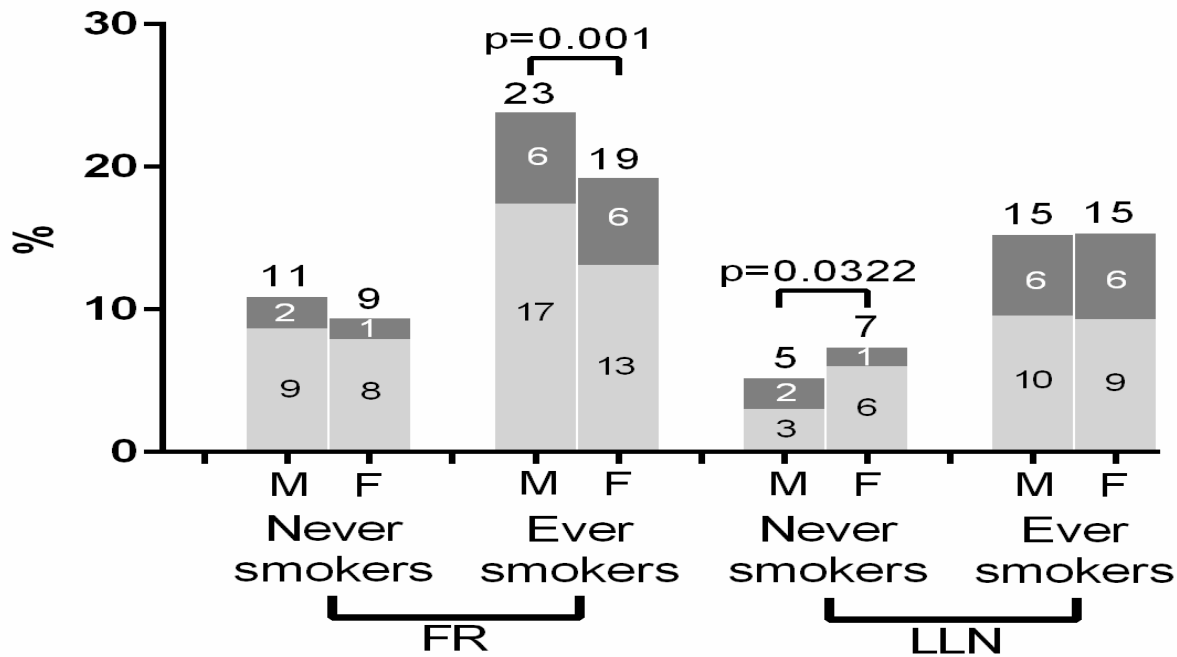
Comments: The prevalence defined by Fixed Ratio (FEV1/FVC<0.7) is higher than COPD defined by LLN (FEV1/FVC<LLN). This is as expected and has been shown in many published studies. It is interesting that there is a female bias for COPD in never-smoker and no sex bias for COPD in ever-smokers when LLN criteria COPD is used. The reverse is true when the fixed ratio criteria for COPD is used: there is a male bias for COPD in ever-smokers and no sex bias for COPD in never smokers. It is unclear from these results which definition is superior.

Figure S2: Comparison of proportions of subjects with respiratory symptoms &outcomes in never-smoker with moderate-severe COPD (grey column) and ever-smokers with moderate - severe COPD(black column) using GOLD (FR) criteria (top section) and LLN criteria (bottom section). No significance difference between never-smoking COPD and ever-smoking COPD when the condition is moderate-severe.